FGFR2 MUTATION ANALYSIS

JOHN WELSH CARDIOVASCULAR DIAGNOSTIC LABORATORY

FGFR2 gene encodes fibroblast growth factor receptor 2, a member of the transmembrane catalytic receptors that have intracellular tyrosine kinase activity. FGFR amino acid sequence is highly conserved between members and throughout evolution. FGFRs differ from one another in their ligand affinities and tissue distribution. FGFR2 gene contains 17 coding exons and spans a genomic distance of about 120 kb, and has been mapped to chromosome 10q26.13. Multiple alternatively spliced transcript variants encoding different isoforms have been noted for this gene. Mutations in this gene are associated with Crouzon syndrome, Pfeiffer syndrome, Craniosynostosis, Apert syndrome, Jackson-Weiss syndrome, Beare-Stevenson cutis gyrata syndrome, Saethre-Chotzen syndrome, and syndromic craniosynostosis. Diseases associated with FGFR2 include cardiocranial syndrome, and scaphocephaly, maxillary retrusion and mental retardation. FGFR2 mutations demonstrate autosomal dominant inheritance with a broad range of clinical severity both within and between families. Definitive genotype/phenotype correlations have not been described.

The John Welsh Cardiovascular Diagnostic Laboratory offers molecular genetic testing for FGFR2 mutations. Individuals are tested by DNA sequencing of the coding exons of the FGFR2 gene. We strongly recommend initial testing of a clearly affected individual, if available, in order to provide the greatest test sensitivity and clearest interpretation of results for subsequent family members. Genetic counseling is recommended for all individuals.

REASONS FOR REFERRAL

Molecular confirmation of the diagnosis of congenital heart diseases (CHD).

METHODOLOGY

Genomic DNA is analyzed for FGFR2 mutations by DNA sequencing of the coding exons of the FGFR2 gene, as well as the exon/intron junctions and a portion of the 5' and 3' untranslated region. Patient DNA is sequenced in both the forward and reverse orientations. If a mutation is identified, additional family members are analyzed only for the familial mutation by automatic fluorescent DNA sequencing.

SERVICE FEES

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<th>Direct and Institutional Billing</th>
<th>CPT Codes</th>
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<tr>
<td>Index Case (Male or Female)</td>
<td>$1,200 per sample</td>
<td>81406</td>
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<tr>
<td>Additional Family Members</td>
<td>$300 per sample; known familial mutation only</td>
<td>81403</td>
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SENSITIVITY

DNA Sequencing Analysis: Approximately 99 percent detection of mutations in the coding exons 2-18 of FGFR2.

SPECIMEN REQUIREMENTS

Blood (preferred): EDTA (purple-top) tubes: Adult: 5 cc  Child: 5 cc  Infant: 2-3 cc
Tissue: Frozen (preferred), RNAlater
Other Body Fluids or Formalin-fixed, Paraffin-embedded Tissue: Call to inquire